UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,521	12/21/2000	Darrel R. Galloway	22727/04079	9991

22245 7590 05/07/2003

NAVAL MEDICAL RESEARCH CENTER
ATTN: (CODE 00L)
503 ROBERT GRANT AVENUE
SILVER SPRING, MD 20910-7500

EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	17

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/747,521	Applicant(s) GALLOWAY ET AL.	
	Examiner Khatol S Shahnan-Shah	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,26,27,31,41,42 and 45-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,26,27,31,41,42 and 45-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicants' preliminary amendment C, received 12/17/2002, paper # 14 is acknowledged. Claims 25, 28-30,32-40, 43-44 were canceled without prejudice. Claims 23, 24, 31, 41 and 42 were amended. New claims 45-50 were added. Specification pages 3, 4, 6, 7, 13 and 15 was amended.

2. Applicants' declaration under 37 CFR 1.132 filed 12/17/2002, paper # 16 is acknowledged. The declaration under 37 CFR 1.132 filed 12/17/2002 by Dr. Darrell R. Galloway is sufficient to overcome the rejection of claim 23-24, 26-27, 31 and 41, 42 and 44 based upon 35 U.S.C. 112, first paragraph and the rejection of claims 23-24, 26-27, 31 and 41-44 under 35 U.S.C. 102 (b), made in paragraphs 11 and 12 of the office action mailed 7/12/2002, paper # 13.

3. Claims 23, 24, 26, 27, 31, 41 - 42 and 45-50 are pending in this application.

Prior Citations of Title 35 Sections

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

5. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 or 1449 has been submitted with this office action.

Drawings

6. Objection to drawings by the Draftsperson under 37 CFR 1.84 or 1.152. has been withdrawn in view of corrected figures 1 and 2.

Abstract

7. Objection to two abstracts of disclosure, i.e. one submitted as page 26 of the original disclosure and another submitted 4/26/2001 paper # 6 is withdrawn. Applicants have canceled one of these abstracts. (Note: The original abstract as page 26 of the original disclosure (12/21/2000) was canceled).

Specification

8. Objection to the specification for not complying with 37 CFR 1.821 (d) is withdrawn in view of applicants' corrections.

Rejections Moot

9. Rejections of claims 43 and 44 35 U.S.C. 112 1st paragraph and 35 U.S.C. 102 (b) made in paragraphs 11 and 12 of the office action mailed 7/12/2002, paper # 13 is moot in view of cancellation of the claims.

Rejections Withdrawn

10. Rejection of claims 23-24, 26-27, 31 and 41-44 are rejected under 35 U.S.C. 102 (b) as being anticipated by Leppela et al. (US Patent No. 5,591,631) is withdrawn in view of applicants' amendments and declaration.

11. Rejection of claims 23, 24, 26, 27, 31, 41 and 42 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicants' amendments and declaration.

New Grounds for Rejection

Specification Informalities

12. The disclosure is objected to because of the following informalities:

Specification pages 5 and 19 contains terms that are misspelled. Page 5 line 20 recites "ceptein redidue" and page 19, line 11 recites "Sores". Appropriate corrections are required.

New Matter Objection to the Specification

13. The amendment filed 12/17/2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: The specific fragments inserted in the specification are creating new matter. Those specific fragments were never contemplated in the specification or the original claims. The amendment to specification now requires that the immunogenic fragment of LF protein comprises amino acids 42-285 of SEQ ID NO: 2, amino acids 34-719 of SEQ ID NO: 2, amino acids 721-809 of SEQ ID NO: 2 and the immunogenic fragment of PA protein comprises amino acids 30-764 of SEQ ID NO: 4, amino acids 204-764 of SEQ ID NO: 4. However the original specification only teaches one immunogenic fragment of LF (amino acids 9-252 of SEQ ID NO: 2) and one immunogenic fragment of PA (amino acids 175-735 of SEQ ID NO: 4) (see page 3 of the specification) the other fragments are not contemplated in the specification and addition of such fragments constitutes a mixing and matching of concepts so as to produce new subgenus that is not described in the specification as filed.

Applicants are required to cancel the new matter in the reply to this Office Action.

New Matter Rejection of the Claims

14. Claims 23, 24, 26, 27, 31, 41 - 42 and 45-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

As to claims 23, 24 and 31 the claims require that the immunogenic fragment of LF protein comprise amino acids 42-285 of SEQ ID NO: 2, amino acids 34-719 of SEQ ID NO: 2, amino acids 721-809 of SEQ ID NO: 2 and the immunogenic fragment of PA protein comprise amino acids 30-764 of SEQ ID NO: 4, amino acids 204-764 of SEQ ID NO: 4. However the specification only teaches one immunogenic fragment of LF (amino acids 9-252 of SEQ ID NO: 2) and one immunogenic fragment of PA (amino acids 175-735 of SEQ ID NO: 4) (see page 3 of the specification) the other fragments are not contemplated in the specification and addition of such fragments constitutes a mixing and matching of concepts so as to produce new subgenus that is not described in the specification as filed. Claim 23 also recites the new limitation " wherein the full –length, mature mutated LF protein comprises a sequence which is the same sequence as the sequence of the full –length, mature wild –type LF protein except for a mutation the eliminates the metalloproteinase activity of the full –length" This new limitation "eliminates the metalloproteinase activity" does not have support in the original description. This issue is the best resolved by applicants pointing to the specification by page and line number where specific written description support for conception of the new claimed invention can be found.

15. Claims 23, 24, 26, 27, 31, 41, 42 and 45-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for one immunogenic fragment of LF (amino acids 9-252 of SEQ ID NO: 2) and one immunogenic fragment of PA (amino acids 175-735 of SEQ ID NO: 4, does not reasonably provide enablement for other immunogenic fragments. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims as amended are extremely broad covering fragments that are not contemplated in the specification. As to claims 23, 24 and 31 these claims require that the immunogenic fragment of LF protein comprises amino acids 42-285 of SEQ ID NO: 2, amino acids 34-719 of SEQ ID NO: 2, amino acids 721-809 of SEQ ID NO: 2 and the immunogenic fragment of PA protein comprises amino acids 30-764 of SEQ ID NO: 4, amino acids 204-764 of SEQ ID NO: 4. However the specification only teaches one immunogenic fragment of LF (amino acids 9-252 of SEQ ID NO: 2) and one immunogenic fragment of PA (amino acids 175-735 of SEQ ID NO: 4) (see page 3 of the specification) the other fragments are not contemplated in the specification.

Applicants arguments filed 12/17/2002 have fully considered and are not persuasive.

Applicants argue, " Claim 23 as amended, recites that the nucleic acid based composition protects mammalian subjects against challenge with lethal toxin of *B. anthracis*. Claim 23 as amended, further recites that the composition comprises a polynucleotide that encodes a full-length, mature, mutated LF protein that lacks metalloproteinase activity or an immunogenic fragment of *B. anthracis* LF protein. Claim 23 further recites that the immunogenic fragment of *B. anthracis* LF protein comprises amino acid 43 through amino acid 285 of SEQ ID NO: 2."

Applicants further argue, " Claim 24 as amended, recites that the nucleic acid based composition comprises a polynucleotide that encodes a full-length, mature, mutated PA protein or an immunogenic fragment of PA protein comprises amino acid 204 through amino acid 764 of SEQ ID NO: 4."

Applicants further argue " Respectfully, applicants are not required to teach optimal amounts in order to meet enablement requirement of 35 USC 112. Applicants are not even required to teach all of the ratios that can be used. All that is required is that the applicant provide sufficient guidance so that one of ordinary skill in the art can make and use the claimed composition without undue experimentation. Applicants have provided examples showing that a one to one ratio of eukaryotic expression plasmids encoding an immunogenic fragment of LF and immunogenic fragment of PA can be used to achieve the desired results."

Applicants further argue "Applicants have conducted studies in the mouse model system, an in vivo model that has been used by others to test the ability of compositions to induce protection against anthrax (see paragraph 2 of Rule 1.132 of Dr. Darrel Galloway). Applicants further argue that applicants are not required to test the compositions recited in claims 23-24 in humans in order to meet the enablement requirement of 112.

It is the examiner's position that new fragments recited in the amended claims 23 and 24 are not enabled by the specification. The specification also does not provide any description of which fragments can be used without loss of immunogenic activity? The specification does not specify where is the position of protective epitope in SEQ ID # 2 or 4? If amino acid 9-252 of SEQ ID # 2 is involved in the protective immunity; it is not clear if this protection extents beyond amino acid 252? The amended claims recite an immunogenic fragment of LF protein comprises amino acids 42-285 of SEQ ID NO: 2, it is not clear if the missing amino acid sequence 9-41 or the new requested shift of the sequence creates any loss in the protective activity of the sequence. Furthermore, no examples of any these fragments are provided. No information, beyond the characterization of PCLF4 and PCPA have been provided by applicants,

which would indicate possession of the claimed fragments. Figure 3 shows fragment 175-764 of PA. It is not clear what has been done with this fragment? The declaration of Rule 1.132 by Dr. Darrel Galloway, only teaches one immunogenic fragment of LF (amino acids 9-252 of SEQ ID NO: 2) and one immunogenic fragment of PA (amino acids 175-735 of SEQ ID NO: 4) which were already taught by the specification. The scope of instant amended claims encompasses fragments, which are not contemplated in the declaration.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variants broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of prediction of protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Therefore, in view of all of the above, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claims.

16. Claims 23, 24, 26, 27, 31, 41, 42 and 45-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what applicants intend in recitation of the term "full length mature mutated " in amended claims 23 and 24.

Conclusions

17. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30am-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith can be reached on (703) 308-3909. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

April 30, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600